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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/090,965	03/04/2002	Friedrich Srienc	110.01480101	6415
26813	7590	01/12/2006	EXAMINER	
MUETING, RAASCH & GEBHARDT, P.A. P.O. BOX 581415 MINNEAPOLIS, MN 55458			PAK, YONG D	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 01/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/090,965	<b>Applicant(s)</b> SRIENC ET AL.	
	<b>Examiner</b> Yong D. Pak	<b>Art Unit</b> 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 27 October 2005.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

The after final response filed on October 27, 2005 has been entered.

Claims 1-13 are pending and are under consideration.

### ***Response to Arguments***

Applicant's amendment and arguments filed on October 27, 2005, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-13 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Madison et al., Johnston et al., Clemente et al., and Linde et al.

Claims 1-13 are drawn to a method of producing PHA in *S. cerevisiae* or *Kluyveromyces* by introducing polynucleotide encoding a PHA<sub>SCL</sub> or PHA<sub>MCL</sub> and a polynucleotide encoding an acetoacetyl-CoA reductase and/or a  $\beta$ -ketothiolase.

Madison et al. teach a method of producing PHA in *S. cerevisiae* by introducing DNA encoding an *A. eutrophus* PHA polymerase (page 44). Madison et al. teach that low levels of PHA was due to insufficient activity of the endogenous  $\beta$ -ketothiolase and acetoacetyl-CoA reductase and points to improving PHA yields in *S. cerevisiae* by increasing the activities of these two enzymes.

Further, Madison et al. teach other PHA<sub>SCL</sub> and PHA<sub>MCL</sub> that can be used in transgenic yeasts (pages 24-35) and that many different transgenic organisms can be used to produce PHA (page 44), such as a *Kluyveromyces*, which also belongs to the family of *Saccharomycetaceae* like *S. cerevisiae*.

The difference between the reference of Madison et al. and the instant invention is that the reference of Madison et al. does not teach a method of producing PHA anaerobically using a yeast transformed a single nucleic construct comprising at least two of  $\beta$ -ketothiolase, acetoacetyl CoA reductase or PHA<sub>SCL</sub> or PHA<sub>MCL</sub>.

However, expression of multiple heterologous genes in yeast is routine in the art. Also, making a single nucleic acid construct composed of more than one or two genes is also very routine in the art (Strategene catalog, cited in previous Office Action). For example, Clemente et al. (U.S. Patent No. 5,489,894 – form PTO-892) discloses a method of expressing three genes via a single nucleic acid construct (Columns 15-16). Johnston et al. discloses using divergent promoters to express more than one gene in *S. cerevisiae*.

Regarding the limitation of producing PHA under anaerobic conditions, it is well known in the art that *S. cerevisiae* is able to grow both aerobically and anaerobically

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(Visser et al., Ohmori et al., Linde et al., Nissen et al.). It is also well known in the art that oxygen can cause serious stress to living organisms, including yeasts (Linde et al. and Nissen et al.). Linde et al. also discloses that gene expression under anaerobic and anaerobic culture conditions showed little difference (page 7412). From the teachings in the art and Linde et al., one having ordinary skill in the art would have recognized to use transgenic *S. cerevisiae* and *Kluyveromyces*, under anaerobic or aerobic conditions, permitting flexibility in culture conditions and thereby improving cost effectiveness of producing PHA.

Therefore, with the references of Madison et al., Johnston et al., Clemente et al., and Linde et al. in hand, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to make a transgenic *S. cerevisiae* or *Kluyveromyces* yeast comprising the heterologous PHA polymerase,  $\beta$ -ketothiolase and/or acetoacetyl CoA- reductase. The motivation of further expressing said enzymes via a single nucleic acid construct is to control and increase activity of said enzymes to increase the yield of PHA. The motivation of producing polyhydroxyalkanoates under anaerobic conditions would be to increase efficiency of the production of polyhydroxyalkanoates. One of ordinary skill in the art would have had a reasonable expectation of success since Madison et al. teach that an increase in activity of  $\beta$ -ketothiolase and an acetoacetyl CoA- reductase in yeast transformed with PHA<sub>SCL</sub> or PHA<sub>MCL</sub> will increase the yield of PHA, Clemente et al. and Johnston et al. both teach expression of multiple genes, and Linde et al. teaches flexibility of expressing genes in

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anaerobic and aerobic culture conditions, thereby improving cost effectiveness of producing PHA.

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that Linde et al. does not particularly suggest flexibility of expressing genes under anaerobic and aerobic conditions since a small number of genes exhibited a greater mRNA levels under aerobic conditions, such as PXA1 and FOX2. While it is true that PXA1 and FOX2 have a greater mRNA levels under aerobic conditions, it does not indicate that all genes involved in B-oxidation will have greater transcription levels under aerobic conditions. Linde et al. demonstrates some genes that prefer aerobic conditions and some genes that prefer anaerobic conditions, but concludes that "aerobic and anaerobic transcript profiles of *S. cerevisiae* exhibit little difference" (page 7412, 2<sup>nd</sup> column). Therefore, one having ordinary skill in the art would have been motivated to express genes involved in PHA synthesis under anaerobic conditions.

Applicants argue that successful production of PHA under anaerobic conditions is surprising because PHA is typically considered an aerobic storage material in microorganism cells and B-oxidation of fatty acids is an aerobic process, and therefore, the instant claims are not obvious. Examiner respectfully disagrees. As applicants have stated in the Remarks (page 3) anaerobic cultures of yeast are well known. Further, Linde et al. teaches little difference of aerobic and anaerobic transcript profiles

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of *S. cerevisiae*. Therefore, one having ordinary skill in the art would have been motivated to culture yeasts under anaerobic or aerobic conditions in order to increase efficiency of the production of polyhydroxyalkanoates or to determine if genes involved in PHA synthesis have different transcript profiles under aerobic or anaerobic conditions. Further, MPEP 2144 states that

“The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant... while there must be motivation to make the claimed invention, there is no requirement that the prior art provide the same reason as the applicant to make the claimed invention.”

Hence, the rejection is maintained.

None of the claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not

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mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Yong D. Pak  
Patent Examiner 1652



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